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09/888,264	06/22/2001	Sean H. Adams	10466/35	8727
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Paul E. Rauch, Ph.D. c/o Brinks Hofer Gilson & Lione P.O. Box 10395 Chicago, IL 60610				
EXAMINER ANGELL, JON E				
ART UNIT 1635		PAPER NUMBER		

DATE MAILED: 10/07/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

## Application No.

09/888,264

## Applicant(s)

ADAMS ET AL.

## Examiner

J. Eric Angell

## Art Unit

1635

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 28 July 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1 and 27-73 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1 and 27-73 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.  
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

### Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some \* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).  
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

### Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

### DETAILED ACTION

1. This Action is in response to the communication filed on 7/28/2003. The amendment has been entered. Claims 1 and 27-73 are pending in the application and are examined herein.
2. Applicant's arguments are addressed on a per section basis. The text of those sections of Title 35, U.S. Code not included in this Action can be found in a prior Office Action. Any rejections not reiterated in this action have been withdrawn as being obviated by the amendment of the claims and/or applicant's arguments.

#### *Claim Rejections - 35 USC § 112, second paragraph*

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1 and 27-73 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Method claims require an active or positive step that accomplishes the goals for the method which were stated in the method's preamble. Independent claims 1, 41, 44, and 59 lack such a step and are confusing because the additional method step(s) is not sufficiently set forth. While minute details are not required in method claims, at least the basic steps must be recited in a positive, active fashion. See Ex parte Erlich, 3 USPQ2d1011, p.1011 (Bd. Pat. App. Int. 1986). The specific problem with the instant claims (1, 41, 44 and 59) is that the steps presented are simply a method of treating a cell/tissue with a compound and analyzing expression (claims 1,

41, 44 and 59) and analyzing mitochondrial membrane potential (claim 1) or membrane potential (claim 59). There is no requirement or active or positive step in the claims that a compound that affects uncoupling is identified. This is indefinite because it leaves the scope of the claim unclear as to whether it is required that the compound is identified. Claims 28-40, 42, 43, 45-58 and 60-73 are dependent claims and are therefore rejected for the same reasons.

Additionally claims 27, 29-37, 60 and 64-70 are indefinite because these claims recite the phrase "wherein the analyzing". This phrase renders the claims indefinite because it is unclear as to which "analyzing" the phrase refers to as the dependent claims encompass both analyzing expression and analyzing membrane potential or mitochondrial membrane potential. Amending the claims to recite "wherein the analyzing expression of a polypeptide comprises" would obviate this rejection.

Claim 41 is also indefinite. The phrase "and having uncoupling activity within the sample" (see claim 41, lines 4-5) renders claim 41 indefinite because it is unclear if the candidate compound or the polypeptide is intended to have uncoupling activity within the sample. Claims 42 and 43 are dependent claims and are therefore rejected for the same reasons.

Claim 42 is indefinite because the phrase, "wherein uncoupling activity is detecting the expression of the polypeptide" is unclear. Specifically, it is unclear how uncoupling activity can be detecting the expression of the polypeptide.

***Claim Rejections - 35 USC § 112, first paragraph***

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1, 27-38, 44-56, 59-71 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

7. The instant claims are drawn to method of identifying compounds that affect uncoupling and encompass analyzing the expression of polypeptides that have at least 90% or at least 95% sequence identity to a polypeptide encoded by SEQ ID NO: 1 or SEQ ID NO: 2. Therefore, the claims encompass analyzing the expression of a large genus of polypeptides of which only one species has been adequately described in the specification.

The Written Description Guidelines for examination of patent applications indicates, "the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species, by actual reduction to practice, or by disclosure of relevant, identifying characteristics, i.e. structure or other physical and/or other chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show applicant was in possession of the claimed genus." (See MPEP 2100-164)

In the instant case, the Applicants have disclosed SEQ ID NO: 1 and SEQ ID NO: 2 both of which encode the human 2-oxoglutarate carrier protein (OGC). Applicants have identified that human OGC "changes mitochondrial membrane potential" (see p. 3, line 24 of the specification). However, applicants have not identified any variants of human OGC which retain the ability to change mitochondrial membrane potential. Specifically, applicants have not described which polypeptides that are at least 90% or at least 95% identical to OGC (but less than 100% identical to OGC) have the ability to change mitochondrial membrane potential. The applicants have not identified which common elements or attributes critical for the polypeptide to have the ability to affect mitochondrial membrane potential. For instance, the critical functional domains which are required for the polypeptide to have an affect on mitochondrial membrane potential have not been identified.

It is noted that in Fiers v. Sugano (25 USPQ2d, 1601), the Fed. Cir. concluded that:

"...if inventor is unable to envision detailed chemical structure of DNA sequence coding for a specific protein, as well as method of obtaining it, then conception is not achieved until reduction to practice has occurred, that is, until after the gene has been isolated...conception of any chemical substance, requires definition of that substance other than by its functional utility."

In the instant case, Applicants have identified SEQ ID NOS: 1-2, which encode human OGC protein which they have shown to have an affect on mitochondrial membrane potential. However, Applicants have not identified any variants of human OGC which would also have an affect on mitochondrial membrane potential and which variants would not have an affect on mitochondrial membrane potential. Therefore, one of ordinary skill in would not be able to envision which variants of human OGC would have an affect on mitochondrial membrane potential and which one would not.

Also, in Vas-Cath Inc. v. Mahurkar (19 USPQ2d 1111, CAFC 1991), it was concluded that:

"...applicant must also convey, with reasonable clarity to those skilled in art, that applicant, as of filing date sought, was in possession of invention, with invention being, for purposes of "written description" inquiry, whatever is presently claimed."

In the application at the time of filing, there is no record or description which would demonstrate conception of any variant polypeptide of human OGC which represent functional variants which have the ability to affect mitochondrial membrane potential, a function critical to the successful completion of the claimed method. Therefore, the claims fail to meet the written description requirement by encompassing polypeptides that are not adequately described in the specification.

8. Additionally, since the claims encompass polypeptides for which there is insufficient written description provided in the specification, one of skill in the art would not know how to make or use the claimed method without performing additional experimentation. Considering the claims encompass a very large genus of polypeptides (i.e., any polypeptide at least 90% identical or at least 95% identical to the one encoded by SEQ ID NO: 1 or SEQ ID NO: 2) and the fact that one of skill in the art could not readily predict which variants that meet the limitations would have the desired ability to affect mitochondrial membrane potential, the amount of additional experimentation required to identify the functional variants is considered to be undue.

9. In addition to the rejection above, claims 59-73 are also rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the method set forth in claim

Art Unit: 1635

59 wherein method comprises analyzing the effect of the compound on mitochondrial membrane potential, does not reasonably provide enablement for the claimed method wherein the effect of the compound on any membrane potential is analyzed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make/use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988).

*Wands* states on page 1404,

"Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in *Ex parte Forman*. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

#### The nature of the invention

The instant claims are drawn to a method for screening for compounds that affect uncoupling comprising contacting a mammalian cell or tissue sample with a candidate compound, analyzing expression of a human OGC polypeptide and analyzing the effect of the compound on membrane potential.

#### The breadth of the claims

The claims are very broad and encompass analyzing the effect of the compound on any membrane potential, not just mitochondrial membrane potential.



The unpredictability of the art and the state of the prior art

The relevant prior art does not recognize that human OGC has any affect on any membrane potential, and in fact, Sanchis et al. (1998, see IDS) indicates that human OGC did not affect mitochondrial membrane potential. Therefore, there is no link between human OGC and any membrane potential in recognized in the prior art. The prior art does recognize that OGC is localized to the mitochondrial inner membrane (see Palmissano 1998, see IDS).

Working Examples and Guidance in the Specification

The specification indicates that human OGC can affect mitochondrial membrane potential (see p. 3, line 24; and Example 1, page 48). Specifically, Example 1 indicates that overexpression of human OGC resulted in the decrease of mitochondrial membrane potential. However, there is no indication that human OGC has any affect on cell membrane potential, nuclear membrane potential, or any other membrane potential other than mitochondrial membrane potential.

Quantity of Experimentation

Considering ~~that~~ that the claims encompass human OGC having an affect on any membrane potential but the specification only indicates that human OGC has an affect on mitochondrial membrane potential, and also considering that the prior art recognizes that OGC is localized to the mitochondrial inner membrane (see Palmissano, IDS) additional experimentation would have to be performed in order to establish a link between human OGC and other types of membrane potential.

Level of the skill in the art

The level of the skill in the art is deemed to be high.

Conclusion

Considering the breadth of the claims, the prior art regarding human OGC, the limited working examples and guidance in the specification; and the high degree of skill required, it is concluded that the amount of experimentation required is undue.

*Conclusion*


No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to J. Eric Angell whose telephone number is (703) 605-1165. The examiner can normally be reached on M-F (8:00-4:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader can be reached on (703) 308-0447. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

J. Eric Angell  
Art Unit 1635

  
JEFFREY FRIEDMAN  
PRIMARY EXAMINER